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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,860	01/06/2006	Hana Golding	65831 (47992)	4611

46037 7590 07/23/2008
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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
07/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,860	GOLDING, HANA	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *2,6,8-11,16,19,20 and 22-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,7,12-15,17,18 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/27/05; 3/29/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group I, claims 1-21, is acknowledged. Further election is acknowledged of an antibody agent that associates with an invasin and decreases invasion of vaccinia virus. The response to the election does not indicate whether the election was made with or without traverse. Lacking arguments regarding the merits of the restriction, the election has been treated as an election without traverse. The claims that read on the elected invention are claims 1, 3-5, 7, 12-15, 17, 18 and 21. Claims 2, 6, 8-11, 16, 19, 20 and 22-29 are withdrawn from consideration being drawn to non-elected subject matter.

Claims Summary

2. The claims are drawn to a method of determining whether a candidate agent modulates invasion of a cell by an invasin, comprising incubating a mixture of at least one cell, a labeled invasin that encodes a detectable label, and a candidate agent. The increase/decrease of detection of the label within the cell indicates that the candidate agent modulates invasion of the cell by the invasin. Specifically, the candidate agent decreases invasion of the cell by the labeled invasin. The labeled invasin is a virus, specifically a vaccinia virus. The detectable label is a fluorescent protein or enzyme. The candidate agent is a monoclonal, a polyclonal or altered antibody. An altered antibody includes antibody fragments described on page 11, lines 13-16. The antibody associates with the labeled invasin. The Office interprets "associates with" to be equivalent to the antibody binding the invasin. Specifically, the cell is a mammalian cell, such as a human cell (lymphoid, pulmonary or intestinal).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-5, 7, 12-15 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Domínguez *et al.* (*Journal of Immunological Methods*, 1998, 220:115-221, "Domínguez") in view of Hooper *et al.* (US Patent 6,451,309, "Hooper"). The claims are summarized above. Domínguez discloses green fluorescent protein (GFP) expressed by a recombinant vaccinia virus that permits early detection of infected cells by flow cytometry (abstract). Domínguez uses the construct as an infection tag and teaches that it is useful for studying tropism in a complex cell population such as porcine PBMCs (page 116, first column, third full paragraph). Domínguez does not disclose the use of the construct for testing the anti-viral activity of candidate agents, particularly antibodies.

However, Hooper teaches the production and identification of vaccinia monoclonal antibodies for the purpose of therapeutic treatment (passive immunization) of vaccinia in humans (abstract). Hooper discloses that potential targets for poxvirus therapeutics, monoclonal antibodies, were generated in mice and tested for their ability to neutralize virus and protect mice from challenge (col. 2, lines 5-20). Hooper teaches that the neutralizing activity of the antibodies was not always predictive of protective efficacy in mice upon challenge.

It would have been obvious to use the vaccinia-GFP construct of Domínguez to test the infectivity of cells in the presence of Hooper's monoclonal antibodies to determine whether the

antibodies are effective agents that inhibit vaccinia virus infectivity. One would have been motivated to use the vaccinia-GFP construct because it shows infectivity, not merely neutralization. As is taught by Hooper, neutralization tests were not always predictive of protective efficacy in mice upon challenge (Hooper, col. 2, lines 14-20). One of ordinary skill in the art would have been motivated to use a method that better reflects the inhibiting activities of the monoclonal antibodies, such as the method described by Domínguez. One would have had a reasonable expectation of success because Domínguez uses a vaccinia construct, and Hooper is testing vaccinia antibodies. One would expect that, in the screening process, Hooper's antibodies (those that are capable of inhibiting vaccinia infection) would bind to the vaccinia-GFP construct of Domínguez (associate with the labeled invasin) and decrease invasion of the cell.

With regard to the limitation of claim 13 which requires that the detectable label be an enzyme, Domínguez discloses that a number of marker genes have been inserted in the vaccinia virus genome, and that their utility has been demonstrated in different experimental situations (thymidine kinase, guanine phosphoribosyl transferase, beta-galactosidase, etc.), see Domínguez, pages 115-116, bridging paragraph. Although Domínguez opts to use GFP, it is clear that enzyme labels are well known in the art to be useful in vaccinia infectivity assays. It would have been well within the ability of the ordinary artisan to elect whether to use GFP or an enzyme label depending on the circumstances of the assay. Therefore, the invention would have been obvious to one of ordinary skill in the art at the time of the invention.

4. Claims 18 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Domínguez *et al.* (*Journal of Immunological Methods*, 1998, 220:115-221, "Domínguez") in view of Hooper *et al.* (US Patent 6,451,309, "Hooper") as applied to claims 1 and 17 above, and further in view of Engelmayer *et al.* (*The Journal of Immunology*, 1999, 163:6762-6768, "Engelmayer"). The claims require that the cell be a human cell, specifically a lymphoid cell, pulmonary cell or intestinal cell. The teachings of Domínguez and Hooper are summarized above, however neither disclose the use of a human cell.

It would have been obvious to test the antibodies of Hooper using the assay of Domínguez in the presence of human cells, such as dendritic cells. Engelmayer analyzes human dendritic cells for their ability to support vaccinia virus infection and replication. Engelmayer discloses that vaccinia virus inhibits the maturation of human dendritic cells and consequently inhibits T cell activation, thus evading the immune system (abstract). Given this information, the artisan that desires to block vaccinia infection/disease in humans (Domínguez and Hooper), would have been motivated to test for antibodies capable of inhibiting vaccinia infection of dendritic cells. One would have had a reasonable expectation of success that Engelmayer's DCs (derived from PBMCs) would have worked in the method of Domínguez because Domínguez uses PBMCs, which are expected to contain DCs. Therefore, the invention would have been obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

5. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B Chen/

Primary Examiner, Art Unit 1648